Health Advisory:

Rabies Threat in Missouri and Limited Human Rabies Vaccine

September 18, 2008

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Health Advisory
September 23, 2008

FROM: **JANE DRUMMOND**
DIRECTOR

SUBJECT: **Rabies Threat in Missouri and Limited Human Rabies Vaccine**

Current Situation

At this time, there exists a limited supply of human rabies vaccine that is normally used for both pre- and post-exposure rabies prophylaxis. The Centers for Disease Control and Prevention (CDC) is not referring to this situation as a "shortage," since there has been no lack of vaccine for individuals in need of treatment after a true rabies exposure. The current situation is a supply limitation in which judicious and appropriate use of rabies vaccine is crucial to ensure the continuing availability of vaccine supplies for those persons most in need.

There are two suppliers of human rabies vaccine in the United States: Novartis (RabAvert®, 1-800-244-7668) and Sanofi Pasteur (Imovax®, 1-800-VACCINE).

Novartis is not currently supplying RabAvert® except for emergency consideration on a case-by-case basis in the event of adverse reactions to alternative vaccination. Novartis will re-direct any customers back to their state/local public health authorities to obtain a pass code to process their order through Sanofi Pasteur.

Sanofi Pasteur will provide Imovax® for post-exposure prophylaxis (PEP) only. To obtain Imovax®, medical providers and pharmacies must first contact their local public health agency or the Missouri Department of Health and Senior Services so that a risk-assessment can be conducted for the suspected exposure. If it is determined that rabies PEP is indicated, a pass code will be provided with which to order vaccine. (The pass code changes on a frequency determined by CDC.) At the time of contact, Sanofi Pasteur will provide the individual ordering vaccine a Rabies Post-Exposure Form. The form must be filled out in its entirety, including the physician's signature and pass code provided by the local health official or the Missouri Department of Health and Senior Services.

Vaccine is not available from either company for rabies pre-exposure use. Pre-exposure vaccination programs will resume when the vaccine supply improves.

Consultation With Local or State Health Departments

Assistance with animal bite/potential rabies exposures may be obtained from local public health agencies (see http://www.dhss.mo.gov/LPHA/LPHAs.html for a list of local public health agencies and contact information) or from the Missouri Department of Health and Senior Services (Monday through Friday, 8:00 AM to 5:00 PM, telephone 573-751-6114 or 24/7 access at 1-800-392-0272). The Missouri Department of Health and Senior Services maintains the Sanofi Pasteur "pass code" for distribution to providers as needed. If they wish, local public health agencies can obtain the pass code from the Missouri Department of Health and Senior Services for distribution to medical providers on a case-by-case basis.

When consulting with local or state public health officials, medical providers should have the following information available:

1. Type of exposure (example: bite, mucous membrane, "bat in the house", etc.).
2. Circumstances surrounding the incident (example: child petting stray cat).
3. Date of incident.
4. Nature of wound (puncture versus scratch, location on body, severity, etc.).
5. Species of animal involved.
6. Patient name, address, telephone number.
7. Animal owner (if applicable) name, address, telephone number.
8. Location of animal following incident.
9. Apparent health and behavior of animal.
10. Rabies vaccination status of animal (if applicable; rabies vaccines are licensed only for dogs, cats, ferrets, horses, cattle, and sheep).
11. Has patient been "previously vaccinated" against rabies? (See "PEP Regimen: Previously Vaccinated Persons" below.)

Reportable Conditions

As a reminder, in accordance with 19 CSR 20-20.020, Reporting Communicable, Environmental and Occupational Diseases (available at http://www.sos.mo.gov/adrules/csr/current/19csr/19csr.asp#19-20), the following conditions are reportable to the local health authority or the Missouri Department of Health and Senior Services:

1. Rabies (Human): Immediately upon first knowledge or suspicion.
2. Animal (mammal) bite, wound, humans: Within one day of first knowledge or suspicion.
3. Rabies (Animal): Within one day of first knowledge or suspicion.
4. Rabies Post-Exposure Prophylaxis (Initiated): Within three days of first knowledge or suspicion.

Why is There an Interruption in Supply?

Starting in June 2007, Sanofi Pasteur began renovating its Imovax® rabies vaccine production facility in France to maintain compliance with the most current requirements from the United States Food and Drug Administration and the French regulatory body. Prior to these renovations, Sanofi Pasteur established an inventory based on historical levels of sales and projected market demand. The facility is scheduled to be approved and operational by mid-to-late 2009. Until the facility is operational, Sanofi Pasteur has a finite amount of Imovax® rabies vaccine. After the renovations began, production problems prevented Novartis from making enough RabAvert® to meet projected rabies vaccine supplies. Consequently, Sanofi Pasteur has been supplying nearly all of the market for rabies vaccine. The increase in demand for Imovax® is outpacing the company's historical levels of supply.

Rabies Risk Assessment

- Rabies risk assessments should be conducted in accordance with *Human Rabies Prevention – United States, 2008, Recommendations of the Advisory Committee on Immunization Practices* (available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e507a1.htm).

- Persons with possible rabies exposure should be evaluated as soon as possible by a health care provider. Providers are encouraged to consult with local and state health officials regarding the need for rabies PEP. Since PEP is an urgent medical issue but not usually an emergency, it can be delayed until animal rabies testing or clinical observation is completed. This approach not only limits administration of PEP to persons with confirmed rabies exposure, but is also cost-saving and conserves limited resources.
- Quarantine of Animals: Quarantine or euthanasia/testing should be used to rule out the need for rabies PEP whenever possible to avoid needless treatment of animal bite victims. Dogs, cats, and ferrets that have bitten a person may be quarantined for a 10-day period beginning with the date of the bite, assuming they are showing no signs of rabies and the bite was provoked. This applies even if the dog, cat, or ferret is not currently vaccinated against rabies. If the dog, cat, or ferret is healthy at the end of this period, it could not have been infectious at the time of the bite. If the dog, cat, or ferret is a stray or unwanted pet, it can be euthanized and tested for rabies in lieu of the 10-day quarantine. Quarantine of other domestic animals such as cattle and horses is determined on a case-by-case basis through consultation with state public health officials. Quarantine periods are not recognized for wild animals or wild-domestic animal crosses (for example, wolf-dog hybrids); they are, instead, euthanized and tested for rabies.
- Animal Rabies Testing: Testing of animals for rabies is conducted only at the State Public Health Laboratory (SPHL) in Jefferson City. Specimens are normally prepared and submitted by veterinarians, county health departments, or animal control agencies. These facilities are equipped to properly prepare the animal sample and have approved shipping containers designed for rabies specimen submission. The State Public Health Laboratory provides a free courier service that picks up boxed specimens each weekday from local health departments and select other facilities. Test results are normally available within one day after delivery to the laboratory. There is no charge for testing, specimen boxes, or courier service. A charge could be incurred if a veterinarian is involved with specimen preparation. Payment of such charges varies by situation (for example, the owner – if there is one – normally pays for veterinary services). More complete rabies testing information may be found at http://www.dhss.mo.gov/Lab/Virology/RabiesTesting.html.
- Bat Exposures: The most common rabies virus variants responsible for human rabies in the United States are bat related; therefore, any potential exposure to a bat requires a thorough evaluation. If possible, bats involved in potential human exposures should be safely collected and submitted for rabies testing. Most bats (approximately 95%) submitted to the SPHL are not rabid and such timely diagnostic assessments rule out the need for unnecessary prophylaxis. The risk of rabies resulting from an encounter with a bat might be difficult to determine because of the limited injury inflicted by a bat bite (compared with more obvious wounds caused by the bite of terrestrial carnivores), an inaccurate recall of a bat encounter that might have occurred several weeks or months earlier, and evidence that some bat-related rabies viruses might be more likely to result in infection after inoculation into superficial epidermal layers. For these reasons, any direct contact between a human and a bat should be evaluated for an exposure. If the person can be reasonably certain a bite, scratch, or mucous membrane exposure did not occur, or if the bat is available for testing and is negative for presence of rabies virus, PEP is not necessary. Other situations that might qualify as exposures include finding a bat in the same room as a person who might be unaware that a bite or direct contact had occurred (e.g., a deeply sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person). These situations should not be considered exposures if rabies is ruled out by diagnostic testing of the bat, or circumstances suggest it is unlikely that an exposure took place. Other household members who did not have direct contact with the bat or were awake and aware when in the same room as the bat should not be considered as having been exposed to rabies. Circumstances that make it less likely that an undetected exposure occurred include the observation of bats roosting or flying in a room open to the outdoors, the observation of bats outdoors or in a setting where bats might normally be present, or situations in which the use of protective covers (e.g., mosquito netting) would reasonably be expected to preclude unnoticed contact. Clustering of human cases associated with bat exposures has

never been reported in the United States (e.g., within the same household or among a group of campers where bats were observed during their activities).

- Rodents and Lagomorphs (rabbits and hares): Rodents and lagomorphs, either wild or domestic, present a very low risk for rabies exposure to humans. While the CDC reports a very small number of rabid wild rodents/lagomorphs each year, there have been no documented cases of transmission of rabies from any of these species to humans in the United States. Each rodent/lagomorph bite to a person should be evaluated individually, but rabies PEP is rarely indicated (even when the biting animal is not available for testing). Medical providers should consult with local or state public health officials regarding these cases as needed.
- Persons at increased risk for rabies exposure should take appropriate precautions to avoid rabies exposure (http://www.cdc.gov/rabies/exposure).

Treatment of Wounds

For many types of bite wounds, immediate gentle irrigation with water or a dilute water povidone-iodine solution markedly decreases the risk for bacterial infection. Wound cleansing is especially important in rabies prevention because thorough wound cleansing alone without other PEP markedly reduces the likelihood of rabies in animal studies. Consideration should be given to the need for a booster dose of tetanus vaccine. Decisions regarding the use of antibiotic prophylaxis and primary wound closure should be individualized on the basis of the exposing animal species, size and location of the wound(s), and time interval since the bite. Suturing should be avoided, when possible.

PEP: General Considerations

- PEP is indicated for persons exposed to a rabid animal.
- Exposures include animal bites or mucous membrane contamination with infectious tissue or fluids such as saliva. Blood, feces, and urine do not contain the virus and are not infectious.
- As noted above, administration of rabies PEP is a medical urgency, not a medical emergency. There have been no vaccine failures in the United States (i.e., someone who developed rabies after vaccination) when PEP was given promptly and appropriately after an exposure.
- Except in extremely high-risk situations, PEP does not have to be immediately administered if the biting animal is available for rabies testing or clinical observation.
- PEP should begin as soon as possible after a thorough risk assessment has been conducted.
- Need for PEP can be ruled out if the animal is determined to be negative for rabies, either by euthanasia and testing or by observing that it remains healthy during a 10-day confinement period. Note: The 10-day confinement period begins with the date of the bite and applies only to dogs, cats, and ferrets.

PEP Regimen: Persons Not Previously Vaccinated

- In the United States, PEP for previously unvaccinated persons consists of a regimen of one dose of human rabies immune globulin (HRIG) and five doses of rabies vaccine over a 28-day period.
- The recommended dose of HRIG is 20 IU/kg body weight. This formula is applicable to all age groups, including children. If anatomically feasible, the full dose should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume should be injected intramuscularly (IM) at a site distant from vaccine administration.
- The HRIG and first dose of vaccine (vaccine is administered IM) should be given as soon as possible after exposure (day 0).
- Additional doses of rabies vaccine should be given on days 3, 7, 14, and 28 after the first vaccination.

- If HRIG was not administered when vaccination was begun (i.e., day 0), it can be administered up to and including day 7 of the PEP series.
- HRIG is not currently in limited supply. It is available from two companies in the United States: Sanofi Pasteur (Imogam®, 1-800-VACCINE) and Talecris Biotherapeutics (HyperRab®, 1-800-243-4153). If rabies PEP is deemed necessary by the medical provider after consultation with local or state public health officials and vaccine is not immediately available, HRIG should be administered as soon as possible following the bite. The full course of five vaccinations should be given as soon as vaccine is available, following the same schedule as noted above, i.e., day 0, 3, 7, 14, 28, with day 0 being the day the first dose of vaccine was administered.
- Current vaccines are relatively painless. Adults should be vaccinated IM in the arm (deltoid area); children should be vaccinated IM in either the deltoid area or the anterolateral aspect of the thigh.
- The gluteal area should never be used for rabies vaccine injections because it may result in lower neutralizing antibody titers.

PEP Regimen: Previously Vaccinated Persons

- Previously vaccinated persons are those who have received one of the recommended pre-exposure or post-exposure regimens of human diploid cell vaccine (HDCV), purified chick embryo cell vaccine (PCECV), or rabies virus adsorbed (RVA), or those who received another vaccine and had a documented rabies virus neutralizing antibody titer.
- These persons should receive 2 IM doses (1.0 mL each in the deltoid) of vaccine, one immediately and one 3 days later.
- HRIG should not be administered to these individuals.
- For previously vaccinated persons who are exposed to rabies, determining the rabies virus neutralizing antibody titer for decision-making about prophylaxis is inappropriate.

Incidence of Rabies in Missouri

Rabies is endemic in wildlife in Missouri, the main reservoirs being bats and skunks. Approximately 50 rabid wild and domestic animals are detected annually in Missouri. However, this number underestimates the true incidence of rabies in Missouri since testing is only conducted in situations that have public health significance (for example, a wild animal has bitten a person or pet). Over the past 10 years (1998-2007), bats have accounted for about 70 percent of the rabid animals detected while skunks accounted for slightly more than 20 percent. The following numbers of other rabid animals were observed during that 10-year period: 8 horses, 6 dogs, 6 cats, 4 cows, 2 foxes, 1 goat, and 1 raccoon (the latter had an equivocal test result). Rabid bats may be found anywhere in Missouri, while rabid skunks are confined primarily to the southern one-half of the state. Additional information pertaining to rabies in Missouri may be found at the following DHSS website: http://www.dhss.mo.gov/Rabies.

Questions should be directed to DHSS' Office of Veterinary Public Health at 573-751-6114, or 1-800-392-0272 (24/7).

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